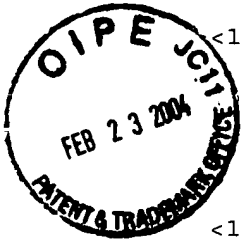


SEQUENCE LISTING



<110> Stegmann, Thomas
Kordyum, Vitaliy A.
Slavchenko, Iryna Yu
Chernykh, Svitlana I
Vozianov, Oleksandr

<120> METHOD OF PRODUCING BIOLOGICALLY ACTIVE
HUMAN ACIDIC FIBROBLAST GROWTH FACTOR AND ITS USE IN
PROMOTING ANGIOGENESIS

<130> CVGENG.008CP1

<140> 10/649,480

<141> 2003-08-27

<150> 09/929,945

<151> 2001-08-15

<150> 60/225,406

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<150> 09/358,780

<151> 1999-07-22

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<223> Chemically synthesized sequence for human acidic
Fibroblast Growth Factor (155 amino acids) using
preferred codons for E. coli

<221> CDS

<222> (122)...(590)

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gagcggataa caattcccct ctagaataaa tttgttttaa ctttaagaag gagatataca 120
t atg gct gaa ggg gaa atc acc acc ttt aca gcg tta acg gag aaa ttt 169
Met Ala Glu Gly Glu Ile Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe

1

5

10

15

aac ctt ccg ccc ggg aat tac aaa aaa ccc aag ctt ctt tac tgc agt 217
 Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser
 20 25 30
 aac gga gga cac ttc ctg cga att ctg cca gat ggc aca gta gat ggg 265
 Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly
 35 40 45
 act cgc gat cgc tcc gac cag cac att cag ctg caa ctc tcg gcc gaa 313
 Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu
 50 55 60
 agc gtt gga gag gtc tat atc aag tcg acg gag act ggc cag tac ctt 361
 Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu
 65 70 75 80
 gcc atg gac acc gat ggg ctt ctg tat ggc tca cag acg cct aac gaa 409
 Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
 85 90 95
 gaa tgc ttg ttt cta gaa aga cta gaa gaa aac cat tac aac acg tac 457
 Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr
 100 105 110
 ata tcg aaa aaa cat gca gag aag aac tgg ttt gta ggc ctt aaa aaa 505
 Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys
 115 120 125
 aat ggt tcc tgt aag cgt gga cca cgg act cac tat ggc caa aag gct 553
 Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala
 130 135 140
 atc ttg ttc ctg cca cta cca gtg agc tcc gac taa g gatccgaatt 600
 Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp *
 145 150 155
 cgagctccgt cgacaagctt gcggccgcac 630

<210> 2

<211> 155

<212> PRT

<213> Homo sapiens

<400> 2

Met Ala Glu Gly Glu Ile Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe
 1 5 10 15
 Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser
 20 25 30
 Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly
 35 40 45
 Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu
 50 55 60
 Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu
 65 70 75 80
 Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu

| | | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|
| | | | | 85 | | | | | 90 | | | | | 95 | | | | | |
| Glu | Cys | Leu | Phe | Leu | Glu | Arg | Leu | Glu | Glu | Asn | His | Tyr | Asn | Thr | Tyr | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | | | |
| Ile | Ser | Lys | Lys | His | Ala | Glu | Lys | Asn | Trp | Phe | Val | Gly | Leu | Lys | Lys | | | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | | | |
| Asn | Gly | Ser | Cys | Lys | Arg | Gly | Pro | Arg | Thr | His | Tyr | Gly | Gln | Lys | Ala | | | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | | | |
| Ile | Leu | Phe | Leu | Pro | Leu | Pro | Val | Ser | Ser | Asp | | | | | | | | | |
| 145 | | | | | 150 | | | | | 155 | | | | | | | | | |

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 <213> Homo sapiens

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 ggggaattaca agaagcccaa actcctctac tgtagcaacg gggggccactt cctgaggatc 120
 cttccggatg gcacagtgga tgggacaagg gacaggagcg accagcacat tcagctgcag 180
 ctcaagtgcg aaagcgtggg ggaggtgtat ataaagagta ccgagactgg ccagtacttg 240
 gccatggaca ccgacgggct tttatacggc tcacagacac caaatgagga atgtttgttc 300
 ctggaaaggc tggaggagaa ccattacaac acctatatat ccaagaagca tgcagagaag 360
 aattggtttg ttggcctcaa gaagaatggg agctgcaaac gcggtcctcg gactcactat 420
 ggccagaaag caatcttggt tctccccctg ccagtctctt ctgattaa 468

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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Chemically synthesized sequence for human acidic
 Fibroblast Growth Factor (134 amino acids) using
 preferred codons for E. coli

<221> CDS
 <222> (122)...(526)

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 gagcggataa caattcccct ctagaataaa tttgttttaa ctttaagaag gagatataca 120
 t atg aat tac aaa aaa ccc aag ctt ctt tac tgc agt aac gga gga cac 169
 Met Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser Asn Gly Gly His
 1 5 10 15
 ttc ctg cga att ctg cca gat ggc aca gta gat ggg act cgc gat cgc 217
 Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly Thr Arg Asp Arg
 20 25 30
 tcc gac cag cac att cag ctg caa ctc tcg gcc gaa agc gtt gga gag 265
 Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu Ser Val Gly Glu
 35 40 45
 gtc tat atc aag tcg acg gag act ggc cag tac ctt gcc atg gac acc 313

| | | | | | | | | | | | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Val | Tyr | Ile | Lys | Ser | Thr | Glu | Thr | Gly | Gln | Tyr | Leu | Ala | Met | Asp | Thr | | |
| 50 | | | | | | 55 | | | | | 60 | | | | | | |
| gat ggg ctt ctg tat ggc tca cag acg cct aac gaa gaa tgc ttg ttt 361 | | | | | | | | | | | | | | | | | |
| Asp | Gly | Leu | Leu | Tyr | Gly | Ser | Gln | Thr | Pro | Asn | Glu | Glu | Cys | Leu | Phe | | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | | |
| cta gaa aga cta gaa gaa aac cat tac aac acg tac ata tcg aaa aaa 409 | | | | | | | | | | | | | | | | | |
| Leu | Glu | Arg | Leu | Glu | Glu | Asn | His | Tyr | Asn | Thr | Tyr | Ile | Ser | Lys | Lys | | |
| | | | | 85 | | | | 90 | | | | | | 95 | | | |
| cat gca gag aag aac tgg ttt gta ggc ctt aaa aaa aat ggt tcc tgt 457 | | | | | | | | | | | | | | | | | |
| His | Ala | Glu | Lys | Asn | Trp | Phe | Val | Gly | Leu | Lys | Lys | Asn | Gly | Ser | Cys | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | |
| aag cgt gga cca cgg act cac tat ggc caa aag gct atc ttg ttc ctg 505 | | | | | | | | | | | | | | | | | |
| Lys | Arg | Gly | Pro | Arg | Thr | His | Tyr | Gly | Gln | Lys | Ala | Ile | Leu | Phe | Leu | | |
| | | | 115 | | | | | 120 | | | | 125 | | | | | |
| cca cta cca gtg agc tcc gac taaggatccg aattcgagct ccgtcgacaa 556 | | | | | | | | | | | | | | | | | |
| Pro | Leu | Pro | Val | Ser | Ser | Asp | | | | | | | | | | | |
| | | | 130 | | | 135 | | | | | | | | | | | |
| gcttgcgggc gcactcgagc accaccacca ccaccactga gatccggctg ctaacaaagc 616 | | | | | | | | | | | | | | | | | |
| ccgaaaggaa gctg 630 | | | | | | | | | | | | | | | | | |

<210> 5
 <211> 135
 <212> PRT
 <213> Homo sapiens

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| <400> 5 | | | | | | | | | | | | | | | | | |
| Met | Asn | Tyr | Lys | Lys | Pro | Lys | Leu | Leu | Tyr | Cys | Ser | Asn | Gly | Gly | His | | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | | |
| Phe | Leu | Arg | Ile | Leu | Pro | Asp | Gly | Thr | Val | Asp | Gly | Thr | Arg | Asp | Arg | | |
| | | | 20 | | | | | 25 | | | | | 30 | | | | |
| Ser | Asp | Gln | His | Ile | Gln | Leu | Gln | Leu | Ser | Ala | Glu | Ser | Val | Gly | Glu | | |
| | | 35 | | | | 40 | | | | | 45 | | | | | | |
| Val | Tyr | Ile | Lys | Ser | Thr | Glu | Thr | Gly | Gln | Tyr | Leu | Ala | Met | Asp | Thr | | |
| 50 | | | | | | 55 | | | | | 60 | | | | | | |
| Asp | Gly | Leu | Leu | Tyr | Gly | Ser | Gln | Thr | Pro | Asn | Glu | Glu | Cys | Leu | Phe | | |
| 65 | | | | 70 | | | | | | 75 | | | | | 80 | | |
| Leu | Glu | Arg | Leu | Glu | Glu | Asn | His | Tyr | Asn | Thr | Tyr | Ile | Ser | Lys | Lys | | |
| | | | 85 | | | | | 90 | | | | | | 95 | | | |
| His | Ala | Glu | Lys | Asn | Trp | Phe | Val | Gly | Leu | Lys | Lys | Asn | Gly | Ser | Cys | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | |
| Lys | Arg | Gly | Pro | Arg | Thr | His | Tyr | Gly | Gln | Lys | Ala | Ile | Leu | Phe | Leu | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | |
| Pro | Leu | Pro | Val | Ser | Ser | Asp | | | | | | | | | | | |
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<210> 6
 <211> 630
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<213> Artificial Sequence

<220>

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Fibroblast Growth Factor (140 amino acids) using
preferred codons for E. coli

<221> CDS

<222> (122)...(544)

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gagcggataa caattcccct ctagaataaa ttttggttaa ctttaagaag gagatataca 120
t atg ttt aac ctt ccg ccc ggg aat tac aaa aaa ccc aag ctt ctt tac 169

Met Phe Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr

1 5 10 15

tgc agt aac gga gga cac ttc ctg cga att ctg cca gat ggc aca gta 217
Cys Ser Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val

20 25 30

gat ggg act cgc gat cgc tcc gac cag cac att cag ctg caa ctc tcg 265
Asp Gly Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser

35 40 45

gcc gaa agc gtt gga gag gtc tat atc aag tcg acg gag act ggc cag 313
Ala Glu Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln

50 55 60

tac ctt gcc atg gac acc gat ggg ctt ctg tat ggc tca cag acg cct 361
Tyr Leu Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro

65 70 75 80

aac gaa gaa tgc ttg ttt cta gaa aga cta gaa gaa aac cat tac aac 409
Asn Glu Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn

85 90 95

acg tac ata tcg aaa aaa cat gca gag aag aac tgg ttt gta ggc ctt 457
Thr Tyr Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu

100 105 110

aaa aaa aat ggt tcc tgt aag cgt gga cca cgg act cac tat ggc caa 505
Lys Lys Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln

115 120 125

aag gct atc ttg ttc ctg cca cta cca gtg agc tcc gac taaggatccg 554
Lys Ala Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp

130 135 140

aattcgagct ccgtcgacaa gcttgcgggc gcactcgagc accaccacca ccaccactga 614
gatccggctg ctaaca 630

<210> 7

<211> 141

<212> PRT

<213> Homo sapiens

<400> 7

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| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Cys | Ser | Asn | Gly | Gly | His | Phe | Leu | Arg | Ile | Leu | Pro | Asp | Gly | Thr | Val |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Asp | Gly | Thr | Arg | Asp | Arg | Ser | Asp | Gln | His | Ile | Gln | Leu | Gln | Leu | Ser |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Ala | Glu | Ser | Val | Gly | Glu | Val | Tyr | Ile | Lys | Ser | Thr | Glu | Thr | Gly | Gln |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Tyr | Leu | Ala | Met | Asp | Thr | Asp | Gly | Leu | Leu | Tyr | Gly | Ser | Gln | Thr | Pro |
| 65 | | | | 70 | | | | | 75 | | | | | | 80 |
| Asn | Glu | Glu | Cys | Leu | Phe | Leu | Glu | Arg | Leu | Glu | Glu | Asn | His | Tyr | Asn |
| | | | 85 | | | | | 90 | | | | | 95 | | |
| Thr | Tyr | Ile | Ser | Lys | Lys | His | Ala | Glu | Lys | Asn | Trp | Phe | Val | Gly | Leu |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Lys | Lys | Asn | Gly | Ser | Cys | Lys | Arg | Gly | Pro | Arg | Thr | His | Tyr | Gly | Gln |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Lys | Ala | Ile | Leu | Phe | Leu | Pro | Leu | Pro | Val | Ser | Ser | Asp | | | |
| | 130 | | | | | 135 | | | | | 140 | | | | |

<210> 8

<211> 154

<212> PRT

<213> Homo sapiens

<400> 8

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| Ala | Glu | Gly | Glu | Ile | Thr | Thr | Phe | Thr | Ala | Leu | Thr | Glu | Lys | Phe | Asn |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Leu | Pro | Pro | Gly | Asn | Tyr | Lys | Lys | Pro | Lys | Leu | Leu | Tyr | Cys | Ser | Asn |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Gly | Gly | His | Phe | Leu | Arg | Ile | Leu | Pro | Asp | Gly | Thr | Val | Asp | Gly | Thr |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Arg | Asp | Arg | Ser | Asp | Gln | His | Ile | Gln | Leu | Gln | Leu | Ser | Ala | Glu | Ser |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Val | Gly | Glu | Val | Tyr | Ile | Lys | Ser | Thr | Glu | Thr | Gly | Gln | Tyr | Leu | Ala |
| 65 | | | | 70 | | | | | 75 | | | | | | 80 |
| Met | Asp | Thr | Asp | Gly | Leu | Leu | Tyr | Gly | Ser | Gln | Thr | Pro | Asn | Glu | Glu |
| | | | 85 | | | | | 90 | | | | | 95 | | |
| Cys | Leu | Phe | Leu | Glu | Arg | Leu | Glu | Glu | Asn | His | Tyr | Asn | Thr | Tyr | Ile |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Ser | Lys | Lys | His | Ala | Glu | Lys | Asn | Trp | Phe | Val | Gly | Leu | Lys | Lys | Asn |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Gly | Ser | Cys | Lys | Arg | Gly | Pro | Arg | Thr | His | Tyr | Gly | Gln | Lys | Ala | Ile |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Leu | Phe | Leu | Pro | Leu | Pro | Val | Ser | Ser | Asp | | | | | | |
| 145 | | | | | 150 | | | | | | | | | | |